Vaccine 31 (2013) 5930–5933

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Infectious disease research investments: Systematic analysis of immunology and vaccine research funding in the UK☆

Joseph R. Fitchett[a,*], Michael G. Head[b], Rifat Atun[c]

[a] King's College School of Medicine, London SE1 9RT, United Kingdom
[b] University College London, Research Department of Infection and Population Health, UCL Royal Free Campus, Rowland Hill Street, London NW3 2PF, United Kingdom
[c] Imperial College Business School and the Faculty of Medicine, Imperial College London, South Kensington Campus, London SW7 2AZ and Harvard School of Public Health, Harvard University, Boston, USA

ARTICLE INFO

Article history:
Received 12 August 2013
Received in revised form 6 October 2013
Accepted 14 October 2013
Available online 25 October 2013

Keywords:
Vaccine
Immunology
Infectious disease
Public health policy
Research investments
Research and development

ABSTRACT

Financing for global health is a critical element of research and development. Innovations in new vaccines are critically dependent on research funding given the large sums required, however estimates of global research investments are lacking. We evaluate infectious disease research investments, focusing on immunology and vaccine research by UK research funding organisations. In 1997–2010, £2.6 billion were spent by public and philanthropic organisations, with £590 million allocated to immunology and vaccine research. Preclinical studies received the largest funding amount £505 million accounting for 85.6% of total investment. In terms of specific infection, "the big three" infections dominated funding: HIV received £127 million (21.5% of total), malaria received £59 million (10.0% of total) and tuberculosis received £36 million (6.0% of total). We excluded industry funding from our analysis, as open-access data were unavailable. A global investment surveillance system is needed to map and monitor funding and guide allocation of scarce resources.

1. Introduction

Vaccines are the most cost-effective health intervention for the prevention of disease [1]. Since their invention, vaccines have been administered to billions of individuals with significant health and economic benefits, particularly to people in low- and middle-income countries [2,3].

Public funders, philanthropic institutions, pharmaceutical companies and biotech companies all play a role in the research and development (R&D) of new vaccines. A WHO–UNICEF analysis estimated that US$76 billion was required for immunisation strategies for 2006 to 2015 among 117 low- and middle-income countries alone [4]. Although, since 2000, international financing of global health has increased substantially [5]; the Global Immunisation Vision and Strategy for 2006–2015 is under funded by US$11–15 billion [6,7].

Since 2007, R&D expenditures have been estimated for global neglected diseases [8]. A recent study, which reviewed 6170 studies accounting for £2.6 billion of investments, documented for the first time in detail research investments for infectious diseases in the UK or for the UK institutions and the global partners involved in infectious disease research [9]. However, annual expenditures on vaccine research have not been estimated [10]. The United Kingdom (UK) is the second largest investor in global health; however, there are no analyses of R&D funding allocated to vaccine research and delivery. Investments by the UK pharmaceutical industry are also poorly documented, primarily due to commercial sensitivity of the data on R&D funding.

In this study, we systematically analyse the financing for vaccine research and immunology of infectious diseases.

2. Methods

We systematically searched databases and websites for information on research investments for the period 1997–2010. We identified 325,922 studies for screening and included 6165 studies in the final analysis (supplementary figure 1). We created a comprehensive database of open-access infectious disease research projects and categories studies and funding by disease, cross-cutting research theme, and categories along the R&D value chain [9]. The R&D categories included: pre-clinical research; phase 1, 2 or 3 trials; product development; and implementation research.

* Corresponding author. at: Department of Infectious Diseases, 2nd Floor Borough Wing, Guy's Hospital Great Maze Pond, London SE1 9RT, United Kingdom.
Tel.: +44 77 45 537687.
E-mail addresses: joseph.fitchett@doctors.org.uk, joseph.fitchett@lshtm.ac.uk (J.R. Fitchett).

0264-410X/$ – see front matter
http://dx.doi.org/10.1016/j.vaccine.2013.10.048

Preclinical research refers to all basic science studies. Clinical trials included phase 1, phase 2 and phase 3 studies. Product development research included new product trials, phase 4 studies and post-marketing research. Implementation research includes all operational, epidemiological, social science and health economics studies. A specific analysis of immunology and vaccine research is presented in this paper due to the significant relevance of host-pathogen interactions to new vaccine development. Further information on detailed methodology is available online (http://researchinvestments.org/data) and published elsewhere [9].

Variables collected included the study title, abstract, funding awarded to the study, lead institution, principal investigator, and the year of award. We included all immunology and vaccine-related studies for infectious diseases where the lead institution was based in the UK. We excluded immunology and vaccine studies not immediately relevant to infectious diseases. Veterinary infectious disease research was excluded unless there was a clear zoonotic component. We excluded open-access data from the pharmaceutical industry, due to paucity of publically available data. All grant funding amounts were adjusted for inflation and reported in 2010 UK pounds. Grants were not modified according to levels of overheads applied to the award. Grants awarded in a currency other than pounds were converted to UK pounds using the mean exchange rate in the year of award.

A team of researchers and the authors sourced data for the study over 3 years (September 2007 to December 2010). Data were categorised between December 2010 and April 2012 and analysed in two steps: between October 2011 and May 2012, and in July 2013. Microsoft Excel software was used for data categorisation. We used fold differences and statistical tests (nonparametric Mann-Whitney rank sum test, K-sample test and nonparametric Wilcoxon signed-rank test) to compare total investment, number of studies, mean grant, and median grant according to specific infection, disease system, funding organisation, and cross-cutting categories. Statistical analysis and generation of figures and graphs were performed using Stata software (v11).

Table 1

3. Results

We identified a total research investment of £590 million across 1276 studies for immunology and vaccine research, accounting for 22.7% of total research investment in infectious diseases, which was £2.6 billion. Funding explicitly for vaccine research amounted to £235 million across 368 studies (9.0% of total).

Diagnostics research accounted for £100.3 million across 407 studies (3.8%) and therapeutics accounted for £408.5 million across 526 studies (15.7%) of total funding of £2.6 billion.

Research with a clear global focus or performed with a partner organisation accounted for £170 million across 264 studies (28.8% of the £590 million for immunology and vaccine research). Figure 1 shows total investment for immunology of infectious diseases and vaccine research studies over time without a clear long-term pattern, with peaks in funding in the years 2000, 2005, 2006 and 2008.

Figure 2 shows total investment for immunology of infectious diseases and vaccine research studies by specific infection. HIV research received the most investment for immunological research with £126.6 million (21.5% of total), followed by malaria with £58.8 million (10.0%) and tuberculosis (TB) with £35.6 million (6.0%). Only 16 out of 45 major infectious diseases (35.6%) included in this analysis received over £1 million funding over the 14-year study period. Pathogens attracting low investment for vaccine research from public and philanthropic funders included Dengue virus, Norovirus, *Clostridium difficile*, *Escherichia coli*, *Neisseria Gonorrhoea*, and *Staphylococci spp.*

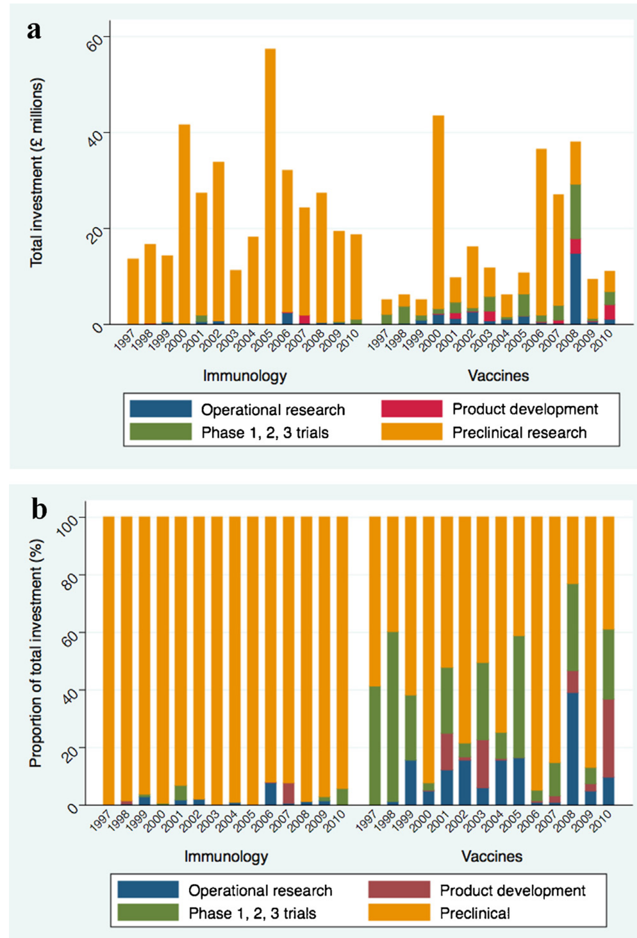

Fig. 1. Bar graph showing: A) total investment in immunology and vaccine research over time by R&D pipeline and B) proportion of investment over time by R&D pipeline.

According to the type of research along the R&D value chain, preclinical research attracted the most investment with £505.1 million (85.6%) followed by phase 1, 2, 3 trials with £41.2 million (7.0%) and implementation research with £31.6 million (5.4%). Product development was the least well-funded type of immunology and vaccine research with £12.5 million (2.1%).

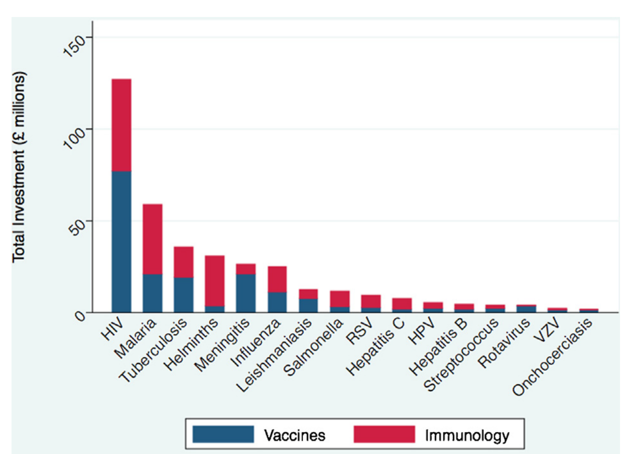

Fig. 2. Bar graph showing total investment in vaccine research by specific infection (for infections with > £1 million research expenditure).

Table 1
Funding for vaccine research and immunology of infectious diseases.

	Infectious disease total ($n = 6165$)			Immunology ($n = 1271$)			Vaccine ($n = 368$)		
	£ (%)	*n* (%)	Median (IQR)	£ (%)	*n* (%)	Median (IQR)	£ (%)	*n* (%)	Median (IQR)
Overall funding	2,599,985,851 (100)	6165 (100)	158,055 (49,490–352,699)	590,183,505 (100)	1271 (100)	203,141 (91,772–409,829)	235,272,456 (100)	368 (100)	226,680 (98,843–589,875)
Preclinical	1,622,545,777 (62.4)	4037 (65.5)	193,149 (74,157–365,587)	505,113,878 (85.6)	1121 (88.2)	202,198 (94,676–396,881)	159,921,393 (68.0)	246 (66.8)	239,727 (107,786–570,651)
Phase 1, 2, 3	146,827,393 (5.6)	145 (2.4)	213,471 (53,116–839,713)	41,039,362 (7.0)	62 (4.9)	269,145 (116,470–1,036,952)	38,113,582 (16.2)	62 (16.8)	250,021 (106,796–774,912)
Product development	132,878,829 (5.1)	335 (5.4)	147,621 (38,625–409,663)	12,475,422 (2.1)	24 (1.9)	196,876 (75,941–706,801)	10,460,905 (4.4)	18 (4.9)	223,741 (68,457–825,550)
Operational research	697,733,852 (26.8)	1648 (26.7)	88,232 (18,513–250,423)	31,554,844 (5.3)	64 (5.0)	151,297 (33,694–394,057)	26,776,576 (11.4)	42 (11.4)	202,911 (62,976–452,939)
Microbiology	2,331,026,142 (90.0)	5380 (87.3)	169,740 (52,373–359,391)	503,038,338 (100)	1044 (100)	221,468 (90,564–458,654)	198,337,432 (100)	321 (100)	221,730 (94,470–578,651)
Bacteriology	588,296,526 (22.6)	1995 (32.4)	162,281 (43,788–306,974)	106,739,486 (21.2)	328 (31.4)	194,633 (83,956–333,141)	52,329,638 (26.4)	135 (42.1)	186,341 (86,947–351,372)
Virology	1,027,385,668 (39.5)	2147 (34.8)	160,555 (49,400–371,794)	277,200,289 (55.1)	491 (47.0)	229,851 (103,768–566,629)	108,946,914 (54.9)	142 (44.2)	294,610 (93,936–590,504)
Parasitology	666,939,464 (25.7)	1067 (17.3)	216,260 (70,194–461,390)	118,172,134 (23.5)	220 (21.1)	258,990 (96,401–555,787)	37,060,881 (18.7)	44 (13.7)	346122 (160,298–1,270,540)
Mycology	48,404,484 (1.9)	171 (2.8)	138,258 (41,162–338,222)	926,429 (0.2)	5 (0.5)	45,528 (34,229–296,635)	0	0	-
Public funding	1,403,579,619 (54.0)	2385 (38.7)	255,992 (127,167–529,610)	293,970,066 (49.8)	471 (37.1)	319,694 (178,939–669,138)	129,225,930 (54.9)	170 (46.2)	361,232 (178,182–760,160)
BBSRC[a]	186,268,429 (7.2)	578 (9.4)	253,398 (169,787–365,159)	46,325,975 (7.8)	153 (12.0)	256,661 (123,344–355,566)	16,031,780 (6.8)	55 (14.9)	274,839 (109,210–396,881)
UK Government	154,438,214 (5.9)	341 (5.5)	110,178 (19,073–206,784)	4,409,838 (0.7)	32 (2.5)	126,387 (19,119–206,784)	1,690,882 (0.7)	12 (3.3)	126,387 (20,461–187,943)
Department of Health	134961745 (5.2)	285 (4.6)	203,544 (72,628–514,066)	9,333,940 (1.6)	20 (1.6)	210,809 (115,619–458,833)	9,050,409 (3.8)	18 (4.9)	229,557 (93,936–523,608)
MRC[b]	672,895,698 (25.9)	962 (15.6)	366,479 (199,287–713,178)	171,420,403 (29.0)	227 (17.9)	465,698 (233,658–878,307)	59,773,451 (25.4)	64 (17.4)	590,489 (311,465–1,039,362)
European Commission	255,015,533 (9.8)	219 (3.6)	439762 (127,419–1,454,941)	62,479,910 (10.6)	39 (3.1)	1,040,540 (159–841–1,679,813)	42,679,408 (18.1)	21 (5.7)	1,281,261 (844,207–2,463,962)
Philanthropic funding	1,102,469,932 (42.4)	2874 (46.6)	146,060 (52,433–286,518)	275,611,267 (46.7)	699 (55.0)	153,858 (78,748–299,148)	89,229,325 (37.9)	156 (42.4)	161,257 (69,750–325,119)
Gates Foundation	220,923,242 (8.5)	39 (0.6)	1,488,432 (628,545–5,576,863)	34,196,740 (5.8)	10 (0.8)	1,509,077 (355,370–5,457,881)	28,738,860 (12.2)	9 (2.4)	628,545 (355,370–3,496,833)
Charity	193,459,157 (7.4)	851 (13.8)	87,318 (27,616–167,829)	37,631,965 (6.4)	200 (15.7)	114,416 (55,892–192,383)	10,427,688 (4.4)	81 (22.0)	112,012 (49,738–174,086)
IAVI[c]	8,893,468 (0.3)	11 (0.2)	305,339 (305,339–1,132,624)	8,893,468 (1.5)	11 (0.9)	305,339 (305,339–1,132,624)	8,893,468 (3.8)	11 (3.0)	305,339 (305,339–1,132,624)
Wellcome Trust	688,087,494 (26.5)	1984 (32.2)	168,434 (66,419–335,557)	203,782,561 (34.5)	489 (38.5)	167,066 (99,591–356,867)	50,062,778 (21.3)	66 (17.9)	244,795 (135,530–981,193)
Other funding	85,042,871 (3.3)	895 (14.5)	28,006 (6,193–98,621)	11,708,705 (2.0)	90 (7.1)	45,790 (11,638–137,759)	7,923,733 (3.4)	31 (8.4)	94,470 (19,058–249,363)

[a] Biotechnology and Biological Sciences Research Council.
[b] Medical Research Council.
[c] International AIDS Vaccine Initiative.

Public funding accounted for £294.0 million across 471 studies (49.8%) with philanthropic funding awarding £275.6 million across 699 studies (46.7%). The major funding organisations to support this work included the Wellcome Trust (34.5%), the Medical Research Council (MRC; 29.0%) and the European Commission (10.6%).

4. Discussion

We present the first detailed analysis of vaccine research funding awarded to UK institutions and their global partners. The trends over the period of analysis do not indicate that an obvious financing strategy is pursued by the funding agencies.

Immunology and vaccine research receives large amounts of funding compared to other scientific disciplines [9]. However, this is likely due to the high costs associated with vaccine development and immunological research. More work is required to estimate the research shortfall for infectious diseases and the cost of inaction on health outcomes.

Our study highlights clear significant differences in the research investment according to specific infectious disease. HIV, malaria and TB dominate the research funding landscape, with very limited investment for immunology and vaccine research allocated to other serious infections.

Preclinical research dominates the R&D funding landscape for immunology and vaccine research. Although an essential part of innovation, strategic measures to promote the translation of basic science into clinical practice could have significant benefits in health outcomes and stimulate greater advances in new technologies to eliminate or eradicate infectious diseases.

Our data does not include contribution from the pharmaceutical industry, which is especially important in vaccine research, as these data are not publically available.

We urge pharmaceutical companies and industry partners to share their detail with the wider scientific community. We have established RESIN: Research Investments in Global Health (www.researchinvestments.org), a public good to document and disseminate research investment data in an online open-access database to benefit academic institutions and pharmaceutical and biotech companies. It is unlikely that divulging past and current research investments would jeopardise current and future research, where commercially sensitive data can be redacted and may help avoid duplication of research investments in global health.

We analysed major funding organisations, including the Wellcome Trust, the MRC and the European Commission. The Bill & Melinda Gates Foundation is also a major funder for vaccine research and delivery, particularly with donations to the GAVI Alliance for making available vaccines in low-income countries. Our analysis is likely to underestimate global financing, as the United States (US) funding agencies such as the National Institutes of Health are not included. Further limitations of our study include difficulties in ascertaining the right proportion of a grant allocated to a specific disease category. This is particularly relevant in co-infection studies.

It is essential that we map, monitor and evaluate vaccine research funding given the importance of vaccines to global health. Data on current investments, coupled with data on disease burden and efficacy of interventions, will help improve allocation of scarce resources. We urge funding organisations to make available financing data on their investment portfolios, as with the clinical trials registry ClinicalTrials.gov, to inform policy on vaccine research.

Acknowledgements

We thank the Infectious Disease Research Network for their contribution to this work, and acknowledge the assistance of the research and development funding agencies for provision of data. We also thank Fatima Wurie, Mary Cooke and Andrew Hayward for their input into earlier work analysing infectious disease research investments and disease burden.

Author contributions: MGH designed the study. JRF undertook data analysis and created the graphs and figures with input from MGH and RA. JRF interpreted the data and wrote the draft and final versions with input from MGH and RA. All authors reviewed and approved the final version. JRF is guarantor of the paper.

Conflict of interest: JRF, MGH and RA are co-founders of "RESIN: Research Investments in Global Health" (http://www.researchinvestments.org) that aims to provide open-access data on research investments. MGH works for the Infectious Disease Research Network, which has supported this work and is funded by the UK Department of Health. JRF has received funds from the Wellcome Trust and is a steering group member for the Infectious Disease Research Network. RA is a member of the Medical Research Council Global Health Group.

Ethical approval: Not required.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2013.10.048.

References

[1] Nossal GJV. Immunology and world health: key contributions from the global community. Ann N Y Acad Sci 2013;1283:1–7.

[2] Ozawa S, Mirelman A, Stack ML, Walker DG, Levine OS. Cost-effectiveness and economic benefits of vaccines in low- and middle-income countries: a systematic review. Vaccine 2012;31:96–108.

[3] Deogaonkar R, Hutubessy R, van der Putten I, Evers S, Jit M. Systematic review of studies evaluating the broader economic impact of vaccination in low and middle income countries. BMC Public Health 2012;12:878.

[4] Bank W. State of the world's vaccines and immunization. Geneva: World Health Organisation; 2009. http://www.who.int/immunization/sowvi/en/

[5] Ravishankar N, et al. Financing of global health: tracking development assistance for health from 1990 to 2007. Lancet 2009;373:2113–24.

[6] Wolfson LJ, et al. Estimating the costs of achieving the WHO-UNICEF Global Immunization Vision and Strategy, 2006–2015. Bull World Health Org 2008;86:27–39.

[7] Peny J-M, Gleizes O, Covilard J-P. Financial requirements of immunisation programmes in developing countries: a 2004–2014 perspective. Vaccine 2005;23:4610–8.

[8] Moran M, et al. G-FINDER – Neglected disease research and development: a five year review; 2012. p. 1–129. http://policycures.org/downloads/GF2012_Report.pdf

[9] Head MG, et al. UK investments in global infectious disease research 1997–2010: a case study. Lancet 2013;13:55–64.

[10] Szucs TD. Health economic research on vaccinations and immunisation practices—an introductory primer. Vaccine 2005;23:2095–103.